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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/035,596	03/05/1998	WALTER H GUNZBURG	GSF98-01	5000

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EXAMINER	
CHEN, SHIN LIN	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 07/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/035,596	Applicant(s) Gunzburg et al.
	Examiner Shin-Lin Chen	Art Unit 1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *May 19, 2003* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1, 2, 9-14, 16-19, 23-28, 31-33, 36-45, 47-54, and 56-94* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 2, 9-14, 16-19, 23-28, 31-33, 36-45, 47-54, and 56-94* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicants' amendment filed 5-19-03 has been entered. Claims 1, 11, 13, 23, 26, 32, 53, 59, 61, 82 and 87 have been amended. Claim 55 has been canceled. Claims 1, 2, 9-14, 16-19, 23-28, 31-33, 36-45, 47-54 and 56-94 are pending and under consideration.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 74-81, 91 and 92 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention and is repeated for the reasons set forth in the preceding Official action mailed 11-15-02 (Paper No. 23). Applicant's arguments filed 5-19-03 have been fully considered but they are not persuasive.

Claims 1, 13, 23 and 26 have been amended, however, claims 74, 79, 91 and 92 have not been amended. Therefore, claims 74-81, 91 and 92 remain rejected under 35 U.S.C. 112 second paragraph.

3. Claims 44 remains rejected and claims 53, 54, 56-65, 68, 69, 71 and 82-90 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention and is repeated

for the reasons set forth in the preceding Official action mailed 11-15-02 (Paper No. 23). Applicant's arguments filed 5-19-03 have been fully considered but they are not persuasive.

Applicants argue that the specification and Kolb reference teach a 320 bp XhoI/XhaI fragment of WAP promoter region is required for mediating the mammary gland specificity and the "proximal 445 bp of the murine WAP promoter" is defined (amendment, p. 5-6). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 11-15-02 (Paper No. 23). Murine WAP promoter encompasses promoter sequences derived from various murine species, i.e. various rat and mouse species, that could be different from the WAP promoter region as disclosed by Kolb reference. It is unclear what proximal 445 bp of which WAP promoter is intended. It is unclear the "proximal 445 bp of the murine promoter" starts from which nucleotide and ends at which nucleotide of a murine WAP promoter region.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1, 2, 9-14, 16-19, 23-28, 31-33, 36-45, 47-54 and 56-94 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for construction of vectors pMMTV-BAG and pWAP-BAG containing β-galactosidase gene under the control of MMTV and WAP, respectively, and the expression of β-galactosidase in explanted normal

primary human mammary tissue infected with virus containing said vectors set forth above, does not reasonably provide enablement for any retroviral vector comprising any therapeutic gene under the control of a MMTV promoter or a WAP promoter and said therapeutic gene is expressed in a cell *in vivo,* a method of expressing said therapeutic gene in a human cell *in vivo*, any pharmaceutical composition comprising a DNA construct, a retrovirus particle, or a cell line, expressing any therapeutic gene under the control of a MMTV promoter or a WAP promoter, and a method for the treatment of human mammary carcinoma comprising administering to a human said pharmaceutical composition expressing any therapeutic gene under the control of a MMTV or WAP promoter *in vivo*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims and is repeated for the reasons set forth in the preceding Official action mailed 11-15-02 (Paper No. 23). Applicant's arguments filed 5-19-03 have been fully considered but they are not persuasive.

Applicants argue that the specification teaches how to make the claimed retroviral vector, retroviral particles, how to infect mammary cells, methods for assessing the activity of WAP or MMTV promoter, preparation of retroviral vector expressing cytochrome P450 under the control of WAP promoter, how to encapsulate a packaging cell and implant the capsule in mammary tissue, and how to obtain or isolate therapeutic genes. Applicants cite In re Wands regarding monoclonal antibody technology and argue that practitioner of the art can not predict which hybridoma would be negative or positive but screening desired hybridoma and *in vivo*

experiment is routine to those skilled in the art, and *in vivo* use of the claimed retroviral vectors to treat a disease is well accepted in the art and no undue experimentation is required for the claimed invention (amendment, p. 7-9). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 11-15-02 (Paper No. 23). The specification fails to provide sufficient enabling disclosure for the full scope of the claimed invention.

As discussed in the preceding Official action mailed 11-15-02, the claims also read on the use of the retroviral vector, the retroviral particle or provirus containing said retroviral vector or the DNA construct set forth above, the packaging cell line comprising said retroviral vector, the human cell containing said retroviral vector and encapsulated cells containing said packaging cell line for gene therapy *in vivo* in light of the specification. The art of gene therapy *in vivo* was unpredictable at the time of the invention. One major obstacle to successful gene therapy *in vivo* has been the inability to deliver genes efficiently and obtain sustained expression. The fate of the DNA vector itself, the *in vivo* consequences of altered gene expression and protein function, the fraction of vector taken up by the target cell population, the trafficking of the genetic material within cellular organelles, the rate of degradation of the DNA, the level of mRNA produced, the stability of the mRNA produced, the amount and stability of the protein produced, and the protein's compartmentalization within the cell, or its secretory fate, once produced are all important factors for a successful gene therapy *in vivo*. In addition, delivery route also plays an important role in efficient gene transfer and sufficient gene expression for gene therapy. The claims encompass any therapeutic gene, including unidentified gene, for gene therapy *in vivo*.

The specification fails to provide correlation between a therapeutic gene and a particular disease or disorder for gene therapy *in vivo*. The specification also fails to provide adequate guidance and evidence for the sufficient expression of any heterologous gene or any therapeutic gene under the control of any MMTV promoter or any WAP promoter in a retroviral vector, a retrovirus particle, cells or encapsulated cells for sufficient duration of time *in vivo* such that therapeutic effects are provided for a particular disease or disorder, or for using said retroviral vector expressing any heterologous gene or therapeutic gene for the treatment of disorders or diseases of human mammary cells *in vivo*. Further, since gene therapy *in vivo* was unpredictable at the time of the invention, each gene therapy case has to be considered case by case. The art of monoclonal antibody technology is different from the art of gene therapy *in vivo*. Screening desired hybridoma is different from gene therapy *in vivo*. The unpredictable nature of gene therapy *in vivo*, the nature of the invention, the state of the prior art, the breadth of the claims, the amount of experimentation necessary, the absence of working examples, and scarcity of guidance in the specification require one skilled in the art undue experimentation to practice over the full scope of the invention claimed.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -

> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

7. Claim 67 remains rejected under 35 U.S.C. 102(e) as being anticipated by Barber et al., 2001 (Us patent No. 6,241,982) and is repeated for the reasons set forth in the preceding Official action mailed 11-15-02 (Paper No. 23). Applicant's arguments filed 5-19-03 have been fully considered but they are not persuasive.

Applicants amended claims 53, 61, 82 and 87 but fail to amend claim 67. Therefore, claim 67 remains rejected under 35 U.S.C. 102(e).

Conclusion

No claim is allowed.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (703) 305-1678. The examiner can normally be reached on Monday to Friday from 9 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds can be reached on (703) 305-4051. The fax phone number for this group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

S/ Chen

Shin-Lin Chen, Ph.D.